



Prospective molecular and morphological assessment of testicular prepubertal-type teratomas in postpubertal men

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Abstract

In 2016, the World Health Organization classification system of testicular tumors included the new entity prepubertal-type teratoma based on its morphological and molecular profile, and the realization that these tumors may occur in postpubertal men. For treatment and prognostic purposes, it is important to distinguish prepubertal-type teratoma from the usual postpubertal-type teratoma, because the former is benign unlike the latter. The distinction may be challenging. In this study, we investigated clinical, morphological, and molecular criteria for distinguishing prepubertal-type teratoma from postpubertal-type teratoma in a prospective series of pure testicular teratomas. All cases of pure teratoma in postpubertal men assessed at Barts Health NHS Trust or in consultation since the introduction of routine investigation of chromosome 12p status in 2010 were reviewed. Morphological features suggestive of prepubertal-type teratoma were observed in 14 out of 35 cases. All underwent molecular testing and none displayed 12p amplification. Mean tumor size was 16 mm (range 7–28 mm). None had associated germ cell neoplasia in situ or significant atrophy. Four incorporated a well-differentiated neuroendocrine tumor, 1–2 mm in size. Of the ten patients with follow-up information, none have recurred or metastasized. Twenty-one of the 35 cases were diagnosed as postpubertal-type teratoma, mean tumor size 40 mm (range 6–90 mm). One case underwent molecular testing: a tumor of pure skeletal muscle differentiation and possessed 12p amplification. Three cases presented with clinical metastases. Eight cases contained immature areas, ten cases had associated germ cell neoplasia in situ, and 17 cases had severe atrophy of the parenchyma. One case with neither germ cell neoplasia in situ nor atrophy showed necrosis. We conclude that both morphological and molecular features are of help in differentiating prepubertal-type teratoma from postpubertal-type teratoma. In nearly all postpubertal-type teratomas, molecular testing was unnecessary, and merely confirmed the morphological impression in the prepubertal-type teratomas. Our study confirmed the high incidence of well-differentiated neuroendocrine tumors in the prepubertal-type.

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Introduction

Diagnosing testicular tumors can be challenging because of their wide range of morphologies. The potential for misdiagnosis of stage and type has been demonstrated in several studies and can cause subsequent mistreatment [1–5]. A fundamental change in the World Health Organization classification system of testicular tumors in 2016 compared with that adopted in 2004, is the distinction of prepubertal-type teratoma from postpubertal-type teratoma [6–8]. This acknowledges separate pathogenesis and the existence of rare benign prepubertal-type teratomas in postpubertal men [9–15], which needs to be recognized by pathologists and treating physicians.

Prepubertal-type teratomas are believed to be derived from a germ cell that has not undergone malignant

transformation [12, 16, 17], and lacks chromosome 12p amplification [12–14]. To our knowledge, there have been no reports of a metastatic or recurrent prepubertal-type teratoma. Therefore, patients with prepubertal-type teratomas require no further treatment other than orchiectomy or local excision, if possible, and can be spared stressful follow-up programmes and potential harms of repeated computer tomography (CT) scans [18, 19]. In contrast, postpubertal-type teratomas are preceded by germ cell neoplasia in situ [20, 21], typically possess 12p amplification [22], and have metastatic potential [21, 23–25]. Therefore, there are two relatively similar morphological tumors that can behave very differently and each with its own treatment and follow-up.

Distinguishing prepubertal-type teratoma from postpubertal-type teratoma in the postpubertal patient may be challenging. Further, due to the small number of published clinic-pathological case studies [9–15, 26], current knowledge of prepubertal-type teratomas in the postpubertal setting is limited. The aim of this study was to investigate the morphological and molecular criteria used to diagnose prepubertal-type teratoma in postpubertal patients.

Materials and methods

All cases diagnosed as pure testicular teratoma in postpubertal men assessed at Barts Health NHS Trust or in consultation since the introduction of routine testing for chromosome 12 abnormalities in 2010 were included and reviewed. Although this entity was not named in 2010, its existence was recognized among expert testicular pathologists and published in 2013 [12]. No previously published cases are included in the present paper. Cases of pure epidermoid cysts were excluded, as distinguishing this entity from postpubertal-type teratoma is usually straightforward, and the evidence of their uniformly benign clinical behavior and lack of germ cell neoplasia in situ and 12p amplification is well described [22, 27–29]. Clinic-pathologic and follow-up data was collected by reviewing the pathology reports and institutional records, and by contacting the referring oncological team. Pathological features recorded included tumor size, different elements of teratoma, any immaturity or atypia, primitive neuroectodermal tumor elements or neuroendocrine elements. When appropriate immunochemistry for Ki-67 was performed on any neuroendocrine component. Stromal features included assessment for the presence of germ cell neoplasia in situ, atrophy, regressive features such as fibrosis and coarse calcification, and necrosis. The postpubertal status of the patients was verified by showing spermatogenesis in all cases. When in doubt, the presence of germ cell neoplasia in situ was assessed by immunohistochemistry for OCT 3/4. We used the strict morphological criteria defined by Zhang et al. [12] to

diagnose a tumor as a prepubertal-type teratoma with absence of all the following features: cytological atypia of the teratomatous elements, germ cell neoplasia in situ, dysgenetic testicular parenchymal changes (significant tubular atrophy/tubular sclerosis, microlithiasis, impaired spermatogenesis and Sertoli-cell-only tubules) [30], and testicular scars.

Molecular testing of chromosome 12p abnormalities by fluorescence in situ hybridization (FISH) was performed on all cases, where a prepubertal-type teratoma was suspected. Unstained 3 μ m sections of formalin fixed, paraffin embedded tissue were received accompanied by an appropriate hematoxylin and eosin stained slide to enable clear identification of tumor areas. Slides were deparaffinised and treated using the SPoT-Light Tissue Pretreatment kit (ThermoFisher) according to manufacturer's instructions. Triple-color FISH was performed by using a mixture of an Aqua-labeled DNA probe for the chromosome 12 centromere (D12Z3), a Texas Red-labeled ETV6 (12p13) DNA probe for chromosome 12p and a FITC-labeled RUNX1 probe (21q22) (Cytocell, Cambridge, UK) according to manufacturer's instructions. The slides were counterstained with 4,6-diamidino-2-phenylindole and cover slipped. The slides were examined using a Zeiss Axioplan Imager 2 microscope and images were acquired and analyzed with MetaSystems Isis software (Germany). A minimum of 100 tumor nuclei were scored independently by two analysts for signals from D12Z3 (aqua) and 12p (red) under the fluorescence microscope with $\times 100$ magnification, and the ratio between red and aqua signals was subsequently calculated. Control probes for the chromosome 12 centromere and chromosome 21 (RUNX1 21q22) were included to help distinguish 12p amplification from polysomy. A positive result for 12p amplification was given if $>10\%$ of nuclei showed three or more ETV6 (12p13) signals relative to the control probes. Sensitivity and specificity studies for the FISH probes were performed on representative tumor tissue as part of validation prior to use. The specificity of the probes was assessed by mapping the chromosomal location on metaphases obtained from peripheral blood from healthy individuals.

The differences in mean age and mean tumor size (as continuous variables) between prepubertal-type teratomas and postpubertal-type teratomas were analyzed using independent *t*-test. Statistical tests were considered significant when $P < 0.05$.

Ethical approval was obtained by Local Ethics Committee (REC No: 09/H0704/4+5).

Results

A total of 35 cases of pure teratoma in postpubertal men were identified out of a total of 474 cases of testicular germ cell tumor between 2010 and 2018.

Prepubertal-type teratomas

Fourteen cases with morphological features suggestive of prepubertal-type teratoma underwent molecular testing, Table 1. Twelve cases displayed no 12p amplification, while the remaining two cases had technical failures. None had associated germ cell neoplasia in situ, signs of regression, or significant atrophy. Four tumors had a small well-differentiated neuroendocrine component, 1–2 mm in size, Fig. 1. The Ki-67 labeling-index of all four well-differentiated neuroendocrine tumors was <2%, and none had tumor necrosis. There was no lymphovascular invasion. The tumors ranged from 7–28 mm (mean: 16 mm) in greatest dimension, and mean tumor size was smaller in prepubertal-type teratomas than in postpubertal-type teratomas (16.2 mm vs. 39.8 mm, $P = 0.004$). Patients ranged from 19–70 years, with a mean age of 38 years, which was no different from the patients diagnosed with postpubertal-type teratomas (38.1 years vs. 35.2 years, $P = 0.56$). One patient (case 5) presented with stage 2 disease, however had a contralateral and synchronous 90 mm seminoma which was treated with chemotherapy. Nine patients either had CT proven clinical stage I disease (eight patients) or on the basis of the diagnosis did not undergo any further tests (one patient). The remaining four patients (referral cases) lacked follow-up information. All ten patients with follow-up information had no evidence of disease progression by physician-verified follow-up at 1–55 months (mean: 15 months); however, the aforementioned patient with a contralateral seminoma was treated with bleomycin–etoposide–cisplatin chemotherapy.

Postpubertal-type teratomas

Twenty cases were diagnosed as postpubertal-type teratomas based on morphology and immunochemistry without molecular investigation, Table 2. One tumor (case 35) without associated germ cell neoplasia in situ or signs of regression underwent molecular testing as it was a tumor of pure mature skeletal muscle differentiation. It was immunohistochemically positive for desmin and smooth muscle actin and displayed 12p amplification. Ten cases had associated germ cell neoplasia in situ, Fig. 2. Nine had no germ cell neoplasia in situ, while in two cases this could not be assessed. Seventeen cases showed severe atrophy or signs of regression in the background parenchyma, while two cases could not be assessed. One case with neither germ cell neoplasia in situ nor severe atrophy or regression showed necrosis. Eight of the tumors had immature areas including primitive neuroectodermal tumor. Three cases presented with disseminated disease. The tumors ranged from 6–90 mm (mean: 40 mm) in greatest dimension. In two cases the tumor size was not stated in the original pathology

report. Patients ranged from 19–67 years of age, with a mean age of 35 years.

Discussion

In the present study, we demonstrate that prepubertal-type teratomas can be distinguished from postpubertal-type teratomas in daily routine practice by careful morphological analysis, supplemented by molecular assessment of 12p amplification, if necessary. Our study confirms that prepubertal-type teratomas can be correctly classified using strict light microscopic morphological criteria, as all the cases with a morphological suspicion of a prepubertal-type teratoma were confirmed as such by lack of 12p amplification (besides two failed tests): morphology correlated with the genetics. An extremely unusual pure skeletal muscle tumor (case 35) did not have associated germ cell neoplasia in situ or signs of regression and therefore one could possibly have had the morphological impression of a prepubertal-type teratoma. It underwent molecular testing due to its unusual morphology. The question is whether testing for chromosome 12p abnormalities is necessary in pure teratoma cases. The technology is not likely to be available in many laboratories. In the case of radical orchiectomy, the distinction between prepubertal-type teratoma and postpubertal-type teratoma based on morphology alone may be more straightforward as it is possible to evaluate the surrounding testis parenchyma for germ cell neoplasia in situ, atrophy and signs of regression. Dysgenetic testicular parenchymal changes which are an exclusion criterion for the diagnosis of prepubertal-type teratoma include significant tubular atrophy/tubular sclerosis, microlithiasis, impaired spermatogenesis, and Sertoli-cell-only tubules [30]. This can be challenging to assess in some cases, as large lesions may show some perilesional atrophy. We suggest that in large tumors, the parenchyma away from the tumor should be assessed if perilesional changes are suspected to be secondary to the size of the lesion.

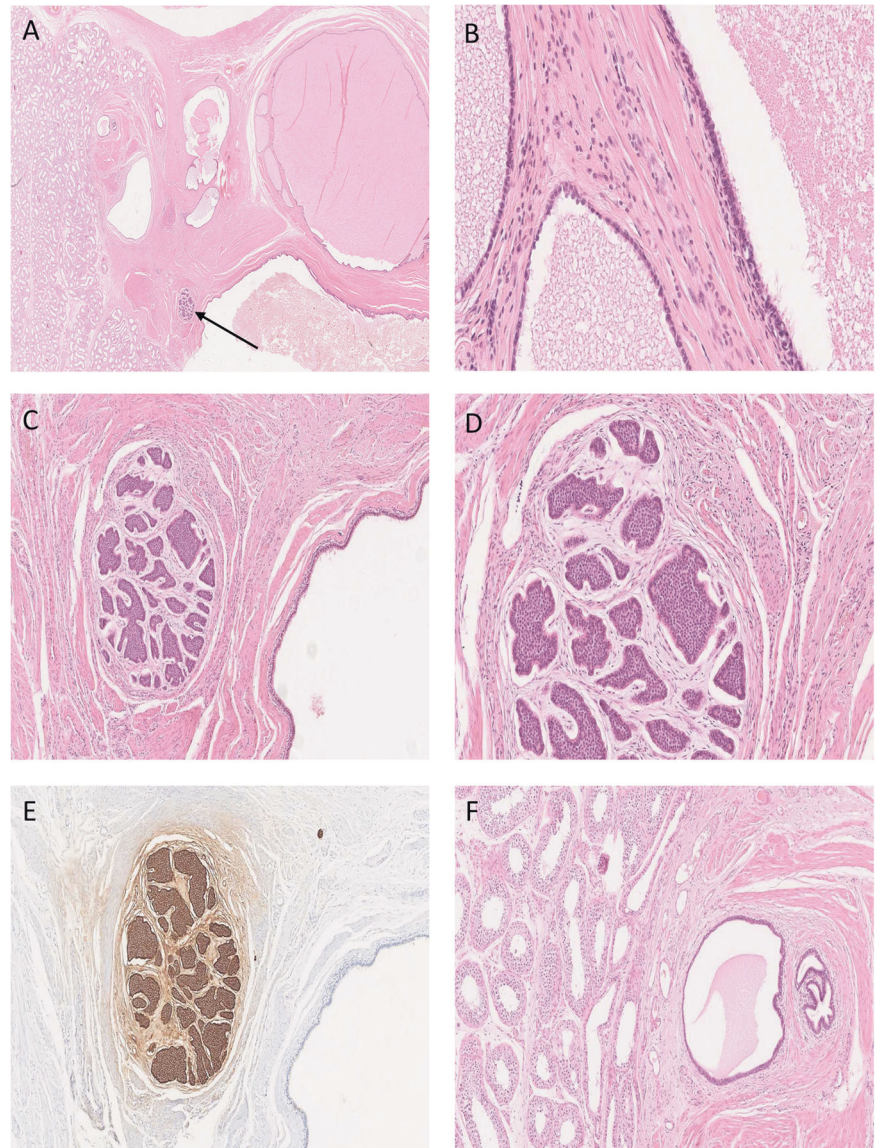
Confirmatory FISH testing may only be needed in challenging cases, such as the pure skeletal muscle tumor. However, we agree with Zhang et al. [12] that an incorrect diagnosis of postpubertal-type teratoma is a more acceptable error than incorrectly diagnosing a prepubertal-type teratoma. Given the limited follow-up data of our cohort, we still recommend performing FISH to confirm absence of 12p amplification when diagnosing a prepubertal-type teratoma in the postpubertal patient, until the morphologic criteria are further validated by additional cases with longer follow-up. The diagnosis of prepubertal-type teratoma is especially challenging on partial orchiectomies, where there may be no parenchyma to assess. When examining a partial specimen, we argue that some surrounding parenchyma and

Table 1 Clinic-pathologic features and follow-up data of cases diagnosed as prepubertal-type teratoma

Case no.	Age	Size (mm)	Histologic findings	Germ cell neoplasia in situ	Regression	Abnormal 12p	Clinical stage	Treatment	F/U (date)	Disease status on last F/U (duration in months)
1	40	18	Smooth muscle, glands, cartilage, 2 mm well-differentiated neuroendocrine tumor with Ki-67 < 2%	No	No	Negative	I	RO, surveillance	A&W (January 2018)	NED (6)
2	24	12	Smooth muscle, bone, glands	No	No	Failed test	NA	RO, NA	NA	NA
3	26	28	Smooth muscle, glands, 1 mm well-differentiated neuroendocrine tumor with Ki-67 < 2%	No	No	Negative	I	RO, surveillance	Discharged (May 2017)	NED (2)
4	64	20	Glands, 2 mm well-differentiated neuroendocrine tumor with Ki-67 < 2%	No	No	Negative	NA	RO, NA	NA	NA
5	42	15	Nevus glands, adnexa, fat tissues	No	No	Negative	II due to contralateral seminoma	RO, chemo	A&W (February 2018)	NED (18)
6	27	7	Glands and smooth muscle	No	No	Negative	I	RO, surveillance	A&W (January 2018)	NED (26)
7	28	15	Squamous epithelium and bone	No	No	Negative	I	RO, surveillance	Discharged (2016)	NED (12)
8	58	20	Squamous epithelium and glands	No	No	Negative	NA	RO, NA	NA	NA
9	46	12	Glands and smooth muscle	No	No	Negative	I	RO, surveillance	Lost to F/U (February 2014)	NED (1)
10	31	10	Mature bone and fibrous tissue	No	No	Failed test	I	RO, surveillance	Discharged (April 2018)	NED (55)
11	33	19	Bone, colonic gland, smooth muscle	No	No	Negative	NA	RO, NA	NA	NA
12	19	17	Squamous, smooth muscle, 2 mm well-differentiated neuroendocrine tumor with Ki-67 of 1%	No	No	Negative	I	RO, surveillance	A&W (January 2019)	NED (12)
13	26	9	Bone, gland	No	No	Negative	Imaging not performed	RO	Discharged without F/U (October 2018)	NED (10)
14	70	25	Squamous, gland, smooth muscle	No	No	Negative	I	RO, surveillance	Discharged (October 2018)	NED (7)

NA not available, RO radical orchiectomy, chemo chemotherapy, NED no evidence of disease, AW alive and well, F/U follow-up

Fig. 1 Well-differentiated neuroendocrine tumor associated with prepubertal-type teratoma. **a** Small well-differentiated neuroendocrine tumor (arrow) surrounded by dilated glands and smooth muscle adjacent to uninvolved tubules seminiferous. **b** High power view of the glands lined by cytologically bland ciliated epithelium. **c, d** The well-differentiated neuroendocrine tumor is composed of solid islands of cells with uniform bland nuclei separated by a fibrous stroma. **e** Labeling for chromogranin is diffuse and strong in the well-differentiated neuroendocrine tumor. **f** Uninvolved seminiferous tubules with only focal tubular atrophy adjacent to the tumor, but otherwise show active spermatogenesis without germ cell neoplasia in situ



absence of 12p abnormalities are required to categorize a tumor as a prepubertal-type teratoma. If this is not possible, the patients should be followed up as a postpubertal-type teratoma. Potential assessment of germ cell neoplasia in situ could be done on a biopsy but, to our knowledge, a study on this has not been performed.

In the present study, four of the prepubertal-type teratomas (case numbers 1, 3, 4, and 12) were associated with a well-differentiated neuroendocrine tumor, compared with no such elements in the postpubertal-type teratomas. Our findings support the 2016 World Health Organization classification system, where testicular neuroendocrine tumors, formerly designated carcinoid tumors, are considered as specialized forms of prepubertal-type teratomas [7, 8]. However, although originally described already in 1954 by Simon et al. [31] the clinical implications of a diagnosis of primary testicular neuroendocrine tumor

associated with teratoma is still somewhat unclear. To our knowledge, only 18 cases of primary neuroendocrine tumor/carcinoid associated with teratoma have been reported in English literature, most consisting of single cases [31–41]. Of the published 18 cases, three had disseminated disease [33, 37, 40]. However, these cases had varied detailed microscopic description of the primary tumors. In 1985, Kaufman et al. described a case of a 43-year-old with a microscopic focus of metastatic carcinoid tumor to a peri-aortic lymph node [37]. The primary tumor size was not mentioned and there was no notion of whether there was atypia, mitosis, or necrosis in the neuroendocrine elements or atypia in the teratomatous component. Further, no description of the surrounding testicular parenchyma. In 2005, Fujita et al. reported a case of a 50-year-old with a 60 mm testicular tumor with metastasis to the para-aortic lymph node of the neuroendocrine elements [40]. The

Table 2 Clinic-pathologic features of cases diagnosed as postpubertal-type teratoma based on morphology and immunochemistry without molecular investigation (except case 35 which underwent molecular testing)

Case no.	Age	Size (mm)	Histologic findings	Germ cell neoplasia in situ	Regression/atrophy	Remarks
15	19	10	Cartilage, glands	Yes	Yes	
16	27	45	Squamous epithelium with atypia and glands	Yes	Yes	
17	38	6	Squamous epithelium, immature glands, and cartilage	No	Yes	
18	23	45	Squamous epithelium, glands, cartilage, and smooth muscle	Yes	Yes	
19	21	18	Glands with atypia, cartilage	Yes	Yes	
20	52	75	Primitive neuroectodermal tumor 75%, glands and smooth muscle	No	Yes	
21	26	55	Glands, fibrous tissue	NA	NA	Presentation with metastasis
22	43	13	Glands with atypia, smooth muscle, cartilage	No	Yes	
23	28	90	Cartilage, focal ganglioneural tissue	NA	NA	Presentation with metastasis
24	67	14	Squamous epithelium, glands with atypia and cartilage	Yes	Yes	
25	54	60	Squamous epithelium and immature glands	No	Yes	
26	29	46	Cartilage, glands, bone, and smooth muscle	Yes	Yes	
27	27	NA	Glands and smooth muscle	Yes	Yes	Partial orchiectomy
28	33	42	Glands, squamous epithelium, glia, cartilage	No	Yes	
29	32	12	Squamous epithelium, bone	No	Yes	
30	35	13	Squamous epithelium, glands, and smooth muscle	Yes	Yes	
31	28	70	Glands, smooth muscle, squamous epithelium	Yes	Yes	Presentation with metastasis
32	22	75	Glands and necrotic areas	No	No	Widespread necrosis in the testicular tumor
33	59	NA	Glands, smooth muscle	No	Yes	
34	30	60	Primitive neuroectodermal tumor 5%, mature elements	Yes	Yes	
35	46	7	Skeletal muscle only	No	No	12p amplification

NA not available

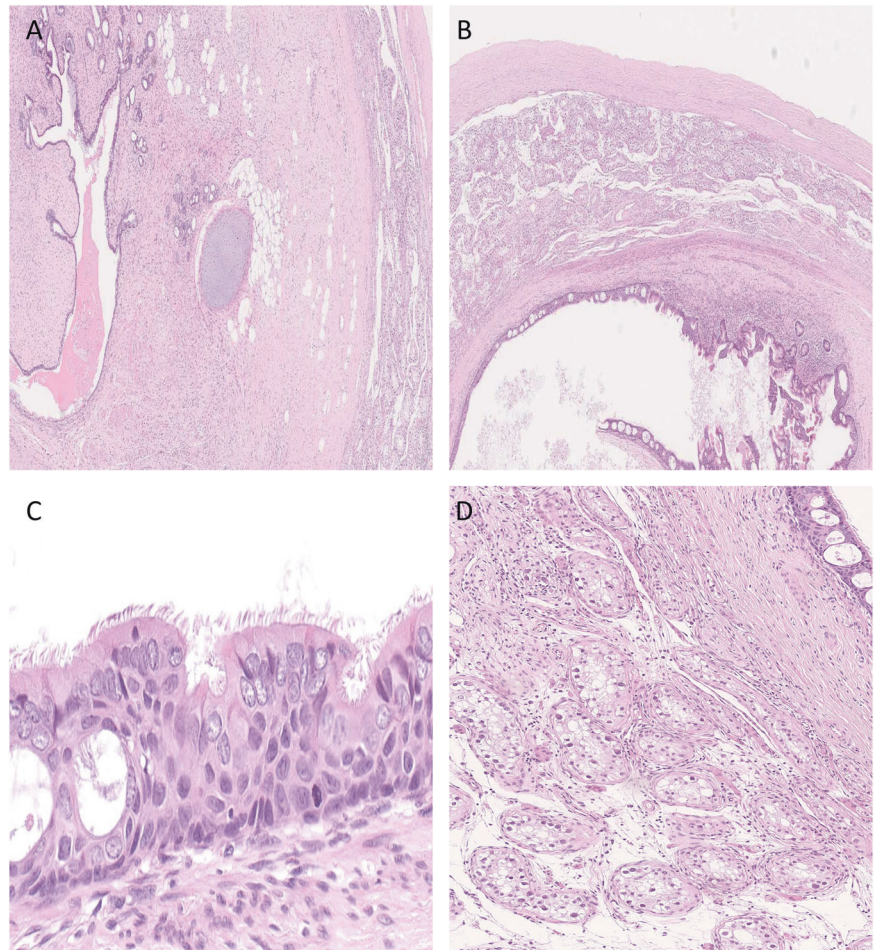
neuroendocrine elements in the primary tumor had areas of atypia and poor differentiation but there was no mention of mitotic rate or presence of necrosis. The teratomatous elements were described as mature with no mention of the surrounding parenchyma. In 2010, Wang et al. reported a case with retroperitoneal and lung metastases who after chemotherapy underwent resection of the retroperitoneal tumor showing metastatic yolk sac tumor and embryonal carcinoma [33]. Although the teratoma component was described as a dermoid, an area of scar was noted, excluding a diagnosis of prepubertal-type teratoma/(dermoid). The neuroendocrine element was described as an atypical carcinoid tumor. No germ cell neoplasia in situ was observed.

Similarly, in the 15 cases without reported metastases, the microscopic description was not sufficiently detailed to assign the cases as prepubertal-type teratoma or postpubertal-type teratoma and whether the associated neuroendocrine components can be categorized as well-differentiated or not. Further, as in our study, the follow-up

data of most of the cases is limited. Therefore, the prognosis of a teratoma associated with neuroendocrine tumor is difficult to interpret in an unequivocal way. It seems plausible to consider two potential factors relating to the prognosis; according to the teratomatous elements (i.e., prepubertal-type teratoma or postpubertal-type teratoma), and according to the neuroendocrine component (well-differentiated or atypical features) [33]. Despite limited follow-up data of the current cases, our findings imply that if the neuroendocrine component is well-differentiated and small with a low Ki-67 index (<2%) and associated with a prepubertal-type teratoma, they may be treated conservatively, bolstered by the absence of 12p amplification in all four tumors included.

The discrepancy in the literature regarding the prognosis is likely due to differences in the pathogenesis of the neuroendocrine elements. Our findings support the theory that primary testicular neuroendocrine tumors are unrelated to germ cell neoplasia in situ [7, 8, 17, 33], as none of the current cases showed this. Only two cases in the literature

Fig. 2 Postpubertal-type teratoma. **a, b** Respiratory epithelium surrounded by smooth muscle, nodule of cartilage, and adipose tissue. **c** High power view of the lining ciliated epithelium with cytological atypia and mitosis. **d** Adjacent seminiferous with germ cell neoplasia in situ



[41, 42], had associated germ cell neoplasia in situ, one of them in a pure carcinoid, in which the tumor was metastatic to a lymph node [42]. Abbosh et al. found that one of four neuroendocrine tumors associated with ‘mature’ teratoma had germ cell neoplasia in situ [41]. They did not report on clinical outcome. However, the description of the surrounding testicular tissue in previous reported cases is sparse and must be interpreted with caution as in eight of the aforementioned 18 cases associated with teratoma [31, 32, 35, 37–40], there were no description; in one case as ‘no significant abnormality’ [34], and another as ‘unremarkable’ [36]. Data regarding cytogenetics are even more limited. To our knowledge, a total of five primary and teratoma-associated neuroendocrine tumors have previously been analyzed for 12p abnormalities. Abbosh et al. identified 12p amplification in both the cells of the neuroendocrine tumor/carcinoid as well as the ‘mature’ teratomatous elements in all four cases [41], suggesting a pathogenesis similar to the postpubertal-type teratoma. Wang et al. examined a carcinoid tumor associated with epidermoid cyst (and therefore not strictly a teratoma associated neuroendocrine tumor) and found no chromosome 12p abnormalities [33]. Similarly, in our study, none of the

tumors displayed 12p amplification. These contradictory findings suggest the possibility of a dual pathogenesis for testicular neuroendocrine tumors [30]. Additional studies are required to investigate this topic. In order to address these challenges, we call for uniformity in the microscopic description of the teratoma component, the surrounding testis parenchyma, 12p status if applicable, as well as a uniform neuroendocrine tumor classification system, including histopathologic grading criteria with description of the tumor cells, presence or absence of necrosis and lymphovascular invasion, mitotic rates, and Ki-67 staining index, as it is done with the tumors in other sites [43, 44].

An additional point that merits a comment is the range of age in the patients diagnosed with prepubertal-type teratomas. It has been speculated that prepubertal-type teratomas presenting in adult life may arise in the prepubertal period but first become clinical manifest or detected at adolescent or adult age [8, 12, 14–16]. In the study of Zhang et al. the tumors occurred over a wide age range of 12–59 years but tended to accumulate in patients in their second and third decades of life [12], suggesting that at least some of them may be previously undetected teratomas that developed prepubertally [15]. Our study showed similar

broad age range (19–70 years), and a tendency of most cases occurring in the second and third decade. However, half of the cases were diagnosed after the fourth decade, including three after the fifth decade, indicating that some of the prepubertal-type teratomas may originate by a similar pathogenetic mechanism as the ones in the prepubertal period but at a later age, as suggested previously by others [12, 14].

Limitations of the study include the limited follow-up: some patients were discharged with no further appointments in view of the favorable prognosis. However, we believe that it is highly likely that in the close networks of testicular pathology in the UK, an unexpected recurrence would have been notified to the authors or clinicians. A further limitation is acquisition bias as many cases are referred to our specialist centre for opinion. This accounts for the high percentage of pure teratomas in the series compared with other centers [21, 45].

In conclusion, in this prospective study we examined 35 cases of pure teratoma in postpubertal men that raised a differential diagnosis between prepubertal-type teratoma and postpubertal-type teratoma and suggest a pathway for correct diagnosis. Both morphological and molecular features are helpful in differentiating prepubertal-type teratoma from postpubertal-type teratoma. Our study demonstrates, that prepubertal-type teratomas may be diagnosed at any age and ancillary 12p testing helps to confirm the morphological suspicion. In nearly all postpubertal-type teratomas molecular testing was unnecessary, and merely confirmed the morphological impression in the prepubertal-type teratomas. Further, our study extends the evidence of the essentially benign nature of prepubertal-type teratomas, emphasizing the importance of the awareness of these small subsets of teratomas in postpubertal men in the setting of therapeutic and prognostic implications for the patients.

Finally, although cases may be biased by referral practice, the high incidence of well-differentiated neuroendocrine tumors only in the prepubertal-type teratomas is confirmed. Optimal methods of follow-up are yet to be determined.

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Compliance with ethical standards

Conflict of interest The authors declare that they have no conflict of interest.

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